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(19)

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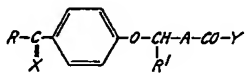
(54) SUBSTITUTED PHENOXY-ALKYL-CARBOXYLIC ACIDS AND DERIVATIVES THEREOF

(71) We, ORCHIMED S.A., a Swiss Body corporate of c/o Me. Gumy, 8 Bd. de Perolles, 1700 Fribourg, Switzerland, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be substantially described in and by the following statement:—

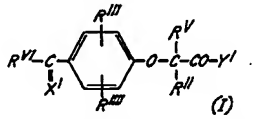
This invention concerns p-carbonyl-phenoxy-carboxylic acids and derivatives thereof which result from transforming the p-oxo radical into oxime, acid, ester and amide radicals and from transforming the carboxylic acid radical into ester and amide radicals.

Our copending Patent Application Number 3085/70 (1 268 321) claims compounds having the formula



where Y is —OH, —OCH_3, —OC_2H_5, —OC_3H_7, NHOH, NR_1R_2, A represents a single bond or a divalent straight- or branched-chain C_{1-3} hydrocarbon radical, R′ is a hydrogen atom or a phenyl group, and either X is = O or = NOH and R is a hydrogen atom or a phenyl, halophenyl, C_{1-3} alkyl, C_{1-3} ω-haloalkyl, and if X = O, R is hydroxyl, methoxy, ethoxy, propoxy, —NHOH or —NR_1R_2 group or R—CX represents a cyano group, each of R_1 and R_2 being a hydrogen atom or an alkyl or diethylamino alkyl group or R_1 and R_2 forming, together with the nitrogen atom to which they are attached, a substituted or unsubstituted heterocyclic group.

The present invention provides compounds having the general formula



(I)

but excluding those claimed in the said copending application, in which R^V and R″ are identical or different and each represents H, CH_3, C_2H_5, C_6H_5, p—F—C_6H_4, p—Cl—C_6H_4, —R‴ and R⁗, which may be identical or different, represent H, a halogen atom, preferably F, Cl or Br, a C_{1-5} alkyl group, CF_3, SCH_3, $SOCH_3$, SO_2CH_3, OCH_3, OH or C_6H_5; R^{VI} represents H, a C_{1-5} alkyl group, an aryl group, an aryl group the aromatic residue of which is substituted by one or more CH_3, CF_3 or halogen atoms, a cycloalkyl group, OH, a C_{1-6} alkoxy group, an aryloxy

group, an aryloxy group the aromatic residue of which is substituted, a cycloalkyloxy group, a NR_3R_4 group, a $NHCH_2CH_2NR_3R_4$ group or an O-alkylene-NR_3R_4 group; Y′ represents OH, C_{1-4} alkoxy, NR_3R_4, $NHCH_2CH_2NR_3R_4$ or O-alkylene-NR_3R_4; X′ represents O or NOR_o; R_o represents H, C_{1-5} alkyl, $CH_2CH_2NR_3R_4$ or $CH_2CHOHCH_2OH$; and each of R_3 and R_4, which may be identical or different, represents a hydrogen atom, a C_{1-5} alkyl group, a C_{5-7} cycloalkyl group, preferably a C_{5-6} cycloalkyl group, an aryl group, an aryl group the aromatic residue of which is substituted by one or more halogen atoms or CF_3 or CH_3 groups, or R_3 and R_4 are joined to form, together with the nitrogen atom to which they are bonded, an optionally substituted 5- to 7-membered heterocyclic ring, which may contain a second hetero-atom selected from O, S and N, or radical of formula $-NH(CH_2)_4CH(NH_2)COOH$ or $-NHCH(COOH)CH_2SH$, with the provisos that if R‴ and R⁗ are not both hydrogen, then R^{VI} is methyl or *p*-chlorophenyl, and that if Y is hydroxy or alkoxy, R^{VI} is hydrogen or C_{1-5} alkyl and one of R″ and and R^V is hydrogen, the other of R″ R^V is methyl or ethyl.

This invention also concerns the acid-addition salts which can be formed from formula I compounds.

Compounds of formula I can be used as therapeutic agents, and act in particular on the central nervous system, or as anti-inflammatory or normolipemiant agents. Such compounds can be used in therapeutic medicines as analgesic, anti-inflammatory, psychotropic, cardiovascular, normolipemiant, hypocholesterolemiant or antitussive ingredients.

Consequently, the invention further provides a therapeutic composition containing at least one compound of the invention as an active ingredient in association with a pharmaceutically acceptable carrier, diluent or coating.

The term alkyl here means a straight or branched hydrocarbon chain. The term alkoxy means a straight or branched hydrocarbon chain which is bonded to an oxygen atom by a single bond. Among the alkoxy groups according to this invention, the following simplest ones can be mentioned: methoxy, ethoxy, propyloxy, isopropyloxy, butyloxy, isobutyloxy and tertiobutyloxy.

The preferred cycloalkyl groups are cyclopentyl, cyclohexyl and $\Delta^{1,2}$-cyclohexenyl. The preferred cycloalkyloxy groups are cyclopentyloxy, cyclohexyloxy and $\Delta^{1,2}$-cyclohexenyloxy.

The term "O-alkylene-NR_3R_4" which is also described as "aminoalkyloxy", represents a group consisting of a divalent straight or branched hydrocarbon chain which is between an oxygen atom and a NR_3R_4 group. Preferably the alkylene residue comprises from 1 to 6 carbon atoms. Among the preferred O-alkylene-NR_3R_4 groups the following ones can be mentioned: aminoethoxy, aminopropyloxy, aminoisopropyloxy, mono- and dialkylaminoethoxy, mono- and dialkylaminopropyloxy, mono- and dialkylaminoisopropyloxy, piperidinoethoxy, azepinoethoxy, morpholinoethoxy, piperazinoethoxy, N′-methylpiperazinoethoxy, pyrrolidinoethoxy, piperidinopropyloxy, piperidinoisopropyloxy, azepinopropyloxy, azepinoisopropyloxy, piperazinopropyloxy, piperazinoisopropyloxy, morpholinopropyloxy, morpholinoisopropyloxy, thiomorpholinopropyloxy, thiomorpholinoisopropyloxy, N′-*p*-chlorophenylpiperazinopropyloxy and N′-*p*-chlorophenylpiperazinoisopropyloxy.

Examples of groups represented by NR_3R_4 are amino, mono- and dialkylamino, morpholino, thiomorpholino, pyrrolidino, piperidino, azepino, N-*p*-chlorophenylpiperazino, N- methylpiperazino, piperazino, 4-methylpiperidino, anilino, N-methylanilino, 2,3-dimethyl anilino, *p*-chloranilino, O-trifluoromethylanilino, *p*-trifluoromethyl anilino, cyclohexylamino and cyclopentylamino groups and analogues thereof.

The preferred halogen atoms are fluorine, chlorine and bromine.

The aryl group of R⁗, R^{VI}, R_3 and R_4 can be substituted by one or more F, Cl, Br, CF_3 and CH_3. The preferred ones according to this invention are phenyl, *p*-chlorophenyl and *p*-fluorophenyl.

Among the compounds corresponding to formula I two kinds of products can be distinguished:

1) the *p*-carbonyl-phenoxy-alkyl-carboxylic acids and derivatives thereof which result

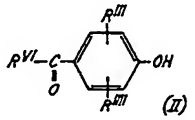
a) from transforming the *p*-oxo group into oxime X = NOR_o,
b) from transforming the carboxylic acid group into ester and amide groups, and,
c) from transforming both the *p*-oxo group into oxime and the carboxylic acid groups into ester and amide groups; and,

2) the *p*-carboxy-phenoxy-alkyl-carboxylic acids, hereafter called "diacids" and derivatives thereof which result from the transformation of one or the both carboxylic acid groups into ester and amide groups.

Among the compounds of the "*p*-carbonyl" type, R^{vi} represents H, C_1—C_8 alkyl, aryl preferably C_6H_5, *p*—Cl—C_6H_4 and *p*—F—C_6H_4.

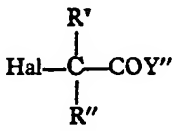
Among the "diacid" type R^{vi} represents OH, C_1—C_6 alkoxy, aryloxy preferably phenoxy and *p*-chlorophenoxy, cycloalkyloxy preferably cyclopentyloxy, cyclohexyloxy, $\Delta^{1,2}$-cyclohexenyloxy, NR_3R_4, $NHCH_2CH_2NR_3R_4$, or O-alkylene-NR_3R_4.

The *para*-carbonyl compounds of formula I in which X′ is an oxygen atom and Y′ is a hydroxy group or a C_{1-3} alkoxy group may be prepared by reacting a *para*-hydroxybenzoyl compound of the formula



(II)

in which R^{vi}, R‴ and R⁗ are defined as above with a halogen compound of the formula



(III)

in which Hal represents a halogen atom, Y″ is a hydroxy group or a C_{1-3} alkoxy group and R^v and R″ are as defined above, in an alkaline medium.

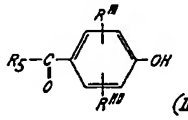
The carbonyl function >C=O may be converted into an oxime function or an ester or other ester or an amide function respectively, using a method known *per-se* for converting a carbonyl function to an oxime function or for converting a carboxylic or C_{1-8} alkoxy ester function to an ester, other ester or amide function.

The following procedures may be used to prepare the compounds of formula I:

PROCEDURE A.

Preparation of acids, esters and amides of formula I, in which R″ is a hydrogen atom and X′ is an oxygen atom

a) A *p*-hydroxybenzoyl derivative having the formula



(IIa)

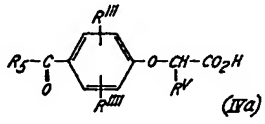
in which R_5 is a hydrogen atom or an alkyl or aryl group, particularly a *p*-chlorophenyl group, is reacted with an α-halogenated acid for the formula

$$R^v—CH(Cl)—CO_2H \qquad \text{(IIIa)}$$

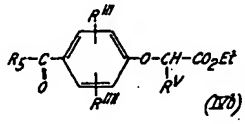
or an α-halogenated ester of the formula

$$R^v—CH(Br)—CO_2Et \qquad \text{(IIIb)}$$

in order to obtain respectively a compound of the formula



(IVa)



(IVb)

b) When R_5 represents a hydrogen atom or an alkyl group, compound IVa may be esterefied using methyl or ethyl alcohol; the ester obtained may be condensed with an appropriate amine to produce a desired amide of formula I, or transesterified to synthesize an ester of formula I other than those already mentioned in procedures A (a) and A (b).

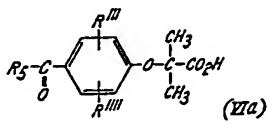
c) When R_5 represents an aryl radical, compound IVa may be converted by means of $SOCl_2$ or PCl_5 into the corresponding acid chloride which may be reacted with an appropriate amine, alcohol or amino alcohol, in accordance with a method known *per se*, in order to obtain respectively a desired amide, ester or amino ester of formula I.

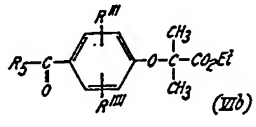
d) Compound IVb may be condensed with an appropriate amine in accordance with a method known *per se* to produce a desired amide of formula I or compound IVb may be transesterified to prepare other esters of formula I.

PROCEDURE A₁

Preparation of acids, esters and amides of formula I in which $R' = R'' = CH_3$ and $X' = O$

a) An acetone-chloroform mixture or an α-halogenated ester of the formula $Br—C(CH_3)_2—CO_2Et$ (V), is reacted with compound IIa in an alkaline medium, in order to obtain respectively a compound of the formula


(VIa)


(VIb)

b) Compound VIa can be esterified by means of a lower alcohol, for instance to give methyl, ethyl or iso-propyl ester, particularly when R_5 is an alkyl group.

c) Ester VIb can be amidified or transesterified, in accordance with methods known *per se* to produce respectively an amide or other ester of the formula I.

d) When R_5 is an aryl group, compound VIa may be converted into the corresponding acid chloride by means of $SOCl_2$ or PCl_5 and then, if desired, the acid chloride may be reacted with an appropriate amine, alcohol or amino-alcohol to produce an amide, ester or amino ester respectively of the formula I.

PROCEDURE B.

Preparation of aldoximes and ketoximes of formula I, i.e. compounds of formula I in which $X' = NOH$ or NOR_o.

a) The compounds of formula I in which $X' = NOH$ may be prepared by treating corresponding compounds of the formula I in which $X' = O$ with hydroxylamine hydrochloride in a basic medium, preferably a pyridinic medium.

b) The compounds of the formula I in which $X' = NOR_o$ may be prepared:— by condensing corresponding compounds of the formula I in which $X' = O$ in a basic (pyridine) medium, with a substituted hydroxylamine hydrochloride, such as:

$$H_2N—O—R_o, HCl,$$

from the compound of the formula I, in which $X' = NOH$, by the following reactions:

$$—NOH \xrightarrow[t.Bu\ OK]{} —NOK \xrightarrow[X\ R_o]{} —NOR_o$$

The following examples are given to illustrate the invention and analogous methods of preparing compounds in accordance with the invention.

EXAMPLE 1.

4-(*p*-chlorobenzoyl)-phenoxy-acetic acid

a) *Preparation of 4-hydroxy-4'-chlorobenzophenone*

Phenol and *p*-chlorobenzoyl chloride are successively added at 0°C to a solution of $AlCl_3$ in nitrobenzene (or a suspension of $AlCl_3$ in ligroine or dichloroethylene); the resulting mixture is kept warm to 25°C for 17 hours, and hydrolysed; 4-hydroxy-4'-chlorobenzophenone is then isolated by extraction using dilute sodium hydroxide and washing with hexane.

b) *4-(p-chlorobenzoyl)-phenoxyacetic acid*

A mixture of 1 mole of 4-hydroxy-4'-chlorobenzophenone, 2.2 moles of NaOH, 1.2 moles of $ClCH_2—CO_2H$ and 1300 cc of water, is refluxed for 7 hours.

After acidification and extraction with $NaHCO_3$ have been conducted and followed by a second acidification, 4-(*p*-chlorobenzoyl)-phenoxyacetic acid is isolated. Its melting point is 152°C.

EXAMPLE 2.

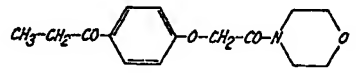
N-(*p*-propionyl-phenoxyacetyl)-morpholine.

This example illustrates the procedures A(b) and A(d) described above.

a) *Methyl p-propionyl-phenoxyacetate*

1 mole of *p*-propionyl-phenoxyacetic acid is refluxed during 10 hours, with 100 cc of MeOH and 300 cc of $CHCl_3$ or CH_2Cl_2 in the presence of sulfuric acid. The resulting mixture is poured into water. The desired ester remains in the organic phase. It is washed once with dilute NaOH, then twice with water. Pure methyl *p*-propionyl-phenoxyacetate is thus isolated, with a yield of about 90%. MP: 59°C.

b)



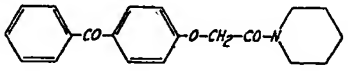
1 mole of the ester obtained in step (a) is refluxed for 8 hours with 2.5 moles of morpholine. Then, 1 volume of water is added, and the product is left to crystallize in the cold state. The morpholinic amide is filtered off and recrystallized from alcohol (yield: 85%; melting point: 88°C).

By using the procedure described in example 2, original compounds listed in table III are prepared.

EXAMPLE 3.

N-(*p*-benzoylphenoxyacetyl)-piperidine

This example illustrates procedure A (c) described above

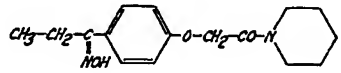


The piperidinoamide of *p*-benzoylphenoxy acetic acid is obtained by treating 1 mole of *p*-benzoylphenoxy acetic acid chloride with 2 moles of piperidine in benzene.

By using the procedure described in example 3, original compounds listed in table IV are obtained.

EXAMPLE 4.

Para-propionhydroximoyl- phenoxy-acetyl-1-piperidine

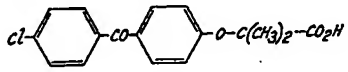


1 mole of *p*-propionylphenoxyacetyl-1-piperidine is refluxed for 5 hours with 1.1 mole of $NH_2OH.HCl$ and 1.05 mole of pyridine. The desired oxime is precipitated in water and recrystallized from alcohol. Its melting point is 144°C.

By using the procedure described in example 4, original compounds listed in table V are obtained.

EXAMPLE 5.

Preparation of para-(4-chlorobenzoyl)-phenoxy-isobutyric acid



1 mole of 4-hydroxy-4'-chlorobenzophenone is dissolved in anhydrous acetone and then 5 moles of powdered sodium hydroxide is added. The corresponding sodium phenate precipitates. Refluxing is effected, and then, 1,5 mole of $CHCl_3$, diluted with anhydrous acetone is added and the resulting mixture is refluxed for 10 hours. After cooling, water is added, the acetone is evaporated, the aqueous phase is washed with ether and acidified and the organic phase is re-dissolved in ether and extracted into a solution of bicarbonate. The bicarbonate solution is then acidified to obtain the desired acid, having a melting point of 185°C, with a yield of 75%.

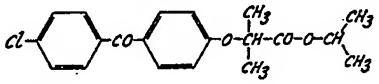
By using the procedure described in example 5, original compounds listed in table VI are prepared.

Esters and amides of the phenoxy-isobutyric acids prepared in accordance with the procedure of example 5 are produced in accordance with procedure A_1 described above. Esters and amides prepared in this manner are listed in table VII.

The compounds listed in table VII can be prepared in a manner similar to that described in the following example.

EXAMPLE 6.

Iso-propyl p-(4-chlorobenzoyl)-phenoxy-isobutyrate



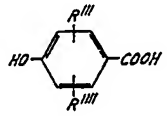
(Code No. 178)

1 mole of the acid obtained in example 6 is converted into its acid chloride using thionyl chloride (2,5 moles). 1 mole of the acid chloride is then condensed with 1,05 mole of isopropyl alcohol in the presence of 0,98 mole of pyridine in an inert solvent such as benzene.

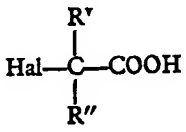
Since traces of SO_2 (which has a bad smell) may be obtained from the thionyl chloride; it is preferable to avoid this disadvantage by carrying out the esterification directly.

Using procedure B described above, isobutyric acids, and esters and amides thereof prepared in example 5 are connected to the corresponding oxime compounds listed in table VIII.

The compounds of formula I in which R^{VI} and Y' are both hydroxy groups may be prepared in accordance with the invention by a) reacting *p*-hydroxybenzoic acid which has the formula



with a halogeno carboxylic acid having the formula

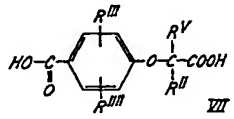


in which Hal represents a halogen atom in an aqueous alkaline medium under reflux, and b) precipitating the resulting diacid in an acidic medium.

It is preferred to use one mole of *p*-hydroxy benzoic acid per mole of the halogeno carboxylic acid.

The compounds of formula I in which at least one of R^{VI} and Y' is other than hydroxyl can be prepared in accordance with the invention by converting at least one of the acid functions of the diacid into an ester or amide function by a method known *per-se* for converting carboxylic acid groups to ester or amide groups.

The diacid, which has the formula



VII

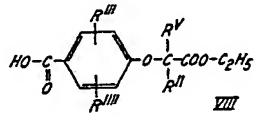
can be used directly:

a) for the synthesis of a diester of the invention in which $R^{VI} = Y'$,

b) to prepare an intermediary acid dichloride for which a diester or a diamide of the invention in which $R^{VI} = Y'$ can be synthesized, or

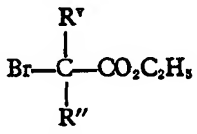
c) for the synthesis of a monoester of the invention; in this case the acid function carried by the oxyacetic chain, i.e. the group $OCR^{V}R''COOH$, is esterified through the acid monochloride prepared with PCl_5 in C_6H_6 at 0°C.

The monoesters of the formula

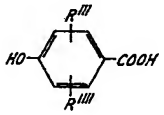


VIII

can be synthesized in accordance with method c) or else by the action of ethyl bromoacetate:

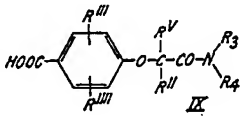


on a *para*-carboxy-hydroxyphenone of the formula



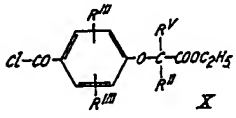
in a heterogenous alkaline medium.

From the monoesters of the invention, particularly those of formula VIII above, there can be obtained, by using a method known *per-se*, monoamides of the invention, e.g. of the formula



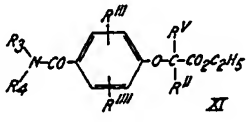
IX

or acid monochlorides, e.g. of the formula



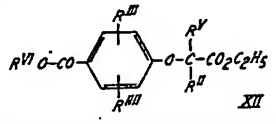
X

The acid monochlorides can in turn be converted into symmetrical and asymmetrical diesters and amide-esters of the invention, e.g. of the formula



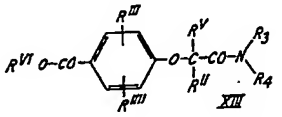
XI

Finally, a symmetrical or asymmetrical diester of the invention, e.g. of the formula



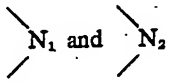
XII

can be converted to an amide ester of the invention, e.g. of the formula

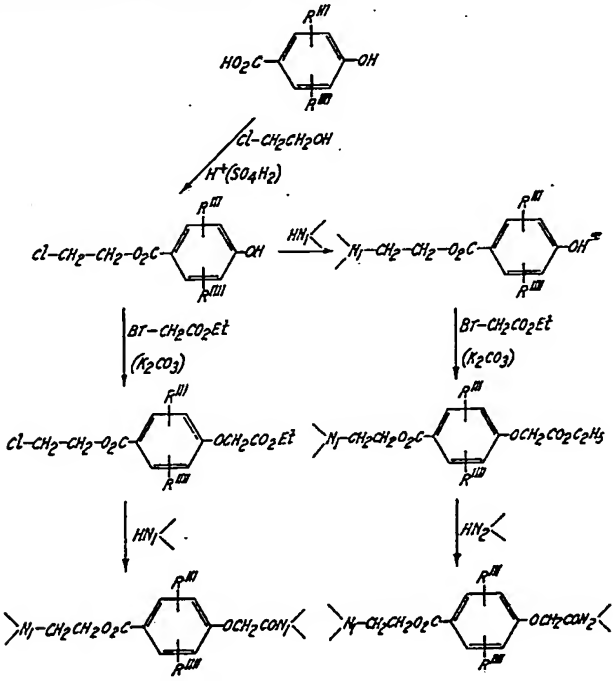


XIII

By a simple modification of the reaction sequences described above it is possible to obtain the compounds of the invention in which one of R^{VI} CO— and —COY′ is an amino-ester group and the other of R^{VI} CO— and —COY is an amide group, any substituents on the nitrogen atom of the amino-ester group being identical to or different from those on the nitrogen atom of the amide group. This is illustrated in the following reaction scheme in which



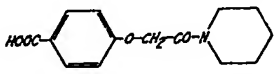
represent non-identical amino groups.



The following examples are given to illustrate the invention.

EXAMPLE 8.

N-(*p*-carboxyphenoxy-acetyl)piperidine

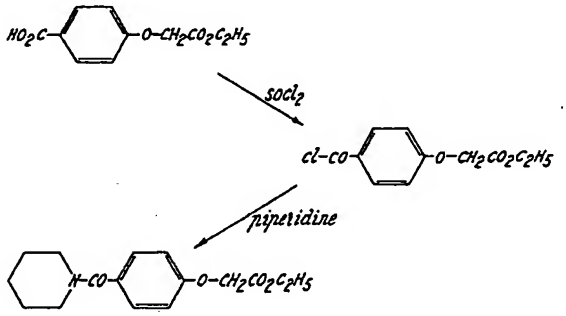


A mixture of 1 mole of ethyl *p*-carboxy-phenoxy-acetate and 2,5 moles of piperidine is refluxed for 7 hours. Water is then added, and 1-*p*-carboxy-phenoxy-acetyl piperidine precipitates.

EXAMPLE 9.

Ethyl para-piperidinocarbonyl-phenoxy-acetate

Operation is in accordance with the following reaction scheme:



The amide ester product can be reacted with any amine, in accordance with the procedure described in Example 8, to produce a diamide.

The substances indicated in Tables I and II are prepared in accordance with the procedure described in Example 8 or Example 9.

The substances listed in Table I bis have been found to possess anti-tussive and analgesic properties.

The following Examples illustrate particular procedures for preparing the compounds number 96 and 99 appearing in Tables I and II respectively.

EXAMPLE 10.

N-(*p*-carboxyphenoxy-acetyl)-piperidine coded as No. 96

a) *Ethyl p-carboxyphenoxy-acetate*

1 mole of ethyl bromoacetate is reacted with 1 mole of *p*-hydroxybenzoic acid in the presence of 2 moles of K_2CO_3 in acetone, methyl-ethylketone, dioxan or tetra-hydrofuran, for 48 hours, at the reflux temperature of the organic solvent to obtain ethyl *p*-carboxyphenoxy-acetate.

b) *N-(p-carboxy-phenoxy-acetyl)piperidine*

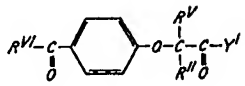
The preceding ester (1 mole) is heated under reflux with piperidine (3 moles) in a chlorinated solvent, for 6 hours. Water is added to precipitate N-(*p*-carboxyphenoxy-acetyl)piperidine after condensation is complete.

EXAMPLE 11.

N-(*p*-ethoxycarbonyl-phenoxy-acetyl)piperidine coded as No. 99

Ethyl *p*-carboxy-phenoxy-acetate is esterified in ethanol and chloroform in the presence of sulphuric acid. N-(*p*-ethoxycarbonyl-phenoxy-acetyl)piperidine is obtained by condensation of 1 mole of the resulting diester (ethyl *p*-ethoxycarbonyl-phenoxy-acetate) with 3 moles of piperidine in an inert solvent for 7 hours at the boiling temperature of said solvent.

TABLE I



Code No.	R^{vi}	R^{v}	R''	Y'	M.P. °C	I.R. cm^{-1} ν–C–R^{vi} ‖ O	I.R. cm^{-1} ν–C–Y' ‖ O	U.V. λ Max.(mμ)	U.V. ε	Activity found
100	$-NH_2$	H	H		168	1630	1660	209 248	19 000 16 000	Anti-inflammatory Anti-tussive
96	–OH	H	H		190	1700	1640	210 249	18 000 17 000	,,
106	$-NH_2$	H	H	$-NH_2$	265	1640	1690	208 251	12 000 15 000	,,
112	–OH	H	H		183	1700	1640	209 248	17 000 16 000	,,
116		H	H	$-OC_2H_5$	90	1630	1760	207 237	14 000 11 000	,,
138	$-NH_2$	H	H		181	1630	1660	208 249	20 000 16 000	,,
145		H	H	$-OC_2H_5$	116	1620	1760	207 241	15 000 12 000	,,

TABLE I (Continued)

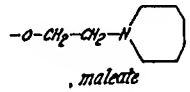
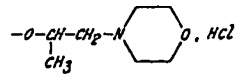
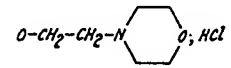
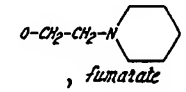
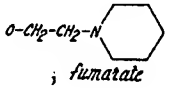
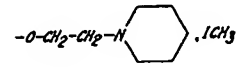
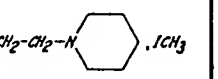
Code No.	R^{vi}	R^{v}	R''	Y'	M.P. °C	I.R. cm^{-1} ν–C–R^{vi} ‖ O	I.R. cm^{-1} ν–C–Y' ‖ O	U.V. λ Max.(mμ)	U.V. ε	Activity found
199	 , *maleate*	H	H	$-OC_2H_5$	75	1710	1760	210 253	27 000 19 000	Anti-tussive, analgesic, cardiovascular
200	$-O-CH_2-CH_2-N(Et)(Et)$, HCl	H	H	$-OC_2H_5$	108	1710	1760	208 255	16 000 20 000	,,
201	 , *HCl*	H	H	$-OC_2H_5$	182	1710	1760	208 253	17 500 20 000	,,
225	 , *HCl*	H	H	$-OC_2H_5$	169	1710	1760	207 254	18 000 19 000	,,
293	 , *fumarate*	H	H	 ; *fumarate*	190	1710	1770	213 252	36 000 22 000	,,
294	 , *ICH3*	H	H	 , *ICH3*	140	1710	1760	217 256	34 000 17 000	,,

TABLE I (Continued)

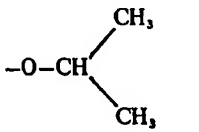
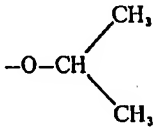
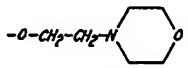
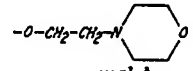
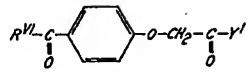
Code No.	R^{vi}	R^{v}	R″	Y′	M.P. °C	I.R. cm^{-1} ν–C–R^{vi} (=O)	I.R. cm^{-1} ν–C–Y′ (=O)	U.V. λ Max.(mμ)	U.V. ε	Activity found
310	–OH	CH_3	CH_3	–OH	175	1690	1700	210 253	15 000 19 000	Antitussive, cardiovascular, normolipemiant
		CH_3	CH_3			1710	1760	–	–	,,
	 , *oxalate*	CH_3	CH_3	 , *oxalate*	136	1710	1730	209 253	15 000 15 000	,,

TABLE II



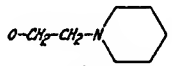
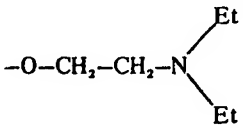
Code No.	R^{vi}	Y'	M.P. °C	I.R. cm^{-1}		U.V.		Activity found
				ν–C–R^{vi} ‖ O	ν–C–Y' ‖ O	λ Max.(mμ)	ε	
99	$-OC_2H_5$		61	1720	1650	216 267	13 000 18 000	Antitussive
105	$-OCH_3$		104	1710	1650	210 253	19 000 19 000	,,
120	$-OC_2H_5$		72	1700	1660	209 252	20 000 20 000	,,
139	$-OCH_3$		110	1710	1660	209 252	19 000 20 000	,,
205	 , *fumarate*		162	1710	1660	210 255	37 000 23 000	Antitussive, analgesic. cardiovascular
204	 HCl		85	1720	1660	209 256	23 000 21 000	,,

TABLE II (Continued)

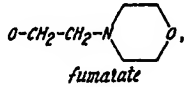
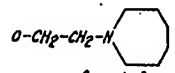
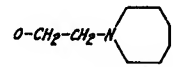
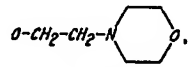
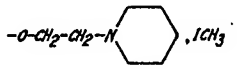
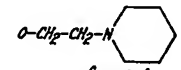
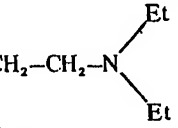
Code No.	R^{vi}	Y'	M.P. °C	I.R. cm^{-1}		U.V.		Activity found
				ν–C–R^{vi} ‖ O	ν–C–Y' ‖ O	λ Max.(mμ)	ε	
221	 *fumarate*		160	1710	1660	210 254	30 000 20 000	Antitussive, analgesic, cardiovascular
222	 *fumarate*		139	1710	1660	210 255	36 000 23 000	,,
228	 *fumarate*		100	1710	1660	207 285	32 000 16 000	,,
235	 *fumarate*		138	1710	1660	209 254	34 000 21 600	,,
249			162	1710	1660	211 242	27 000 30 000	,,
311	 , *fumarate*	 , fumarate	168	1710	1660	212 250	32 000 18 000	,,

TABLE II (Continued)

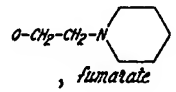
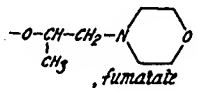
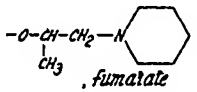
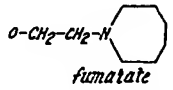
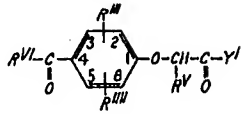
Code No.	R^{vi}	Y'	M.P. °C	I.R. cm^{-1} ν–C–R^{vi} (=O)	I.R. cm^{-1} ν–C–Y' (=O)	U.V. λ Max.(mμ)	U.V. ε	Activity found
312	 , fumarate		134	1710	1660	212 253	31 000 22 000	Antitussive, analgesic, cardiovascular
313	 , fumarate		150	1710	1660	211 252	30 000 22 000	,,
314	 , fumarate		134	1710	1660	211 252	30 000 23 000	,,
	 fumarate		142	1710	1660	212 252	30 000 20 000	,,

TABLE III



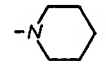
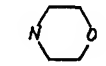
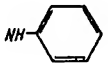
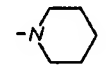
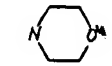
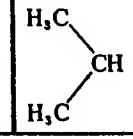
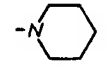
Code No.	R^{vi}	R'''	R''''	R^{v}	Y'	M.P. °C	I.R. cm^{-1}		U.V.		Activity discovered
							ν–C– ‖ O ketone	ν–C– ‖ O amide	λ Max.	ε	
124	CH_3–$(CH_2)_2$	H	H	H		82	1680	1650	213 267	18 000 18 000	Antitussive and psychotropic
126	CH_3–$(CH_2)_2$	H	H	H		76	1680	1650	214 266	18 000 18 000	,,
184	CH_3	H	H	H		130	1700	1665	210 263	18 000 24 000	,,
134	CH_3–CH_2	H	H	H		107	1680	1660	214 266	17 500 17 500	,,
136	CH_3–CH_2	H	H	H		88	1670	enlarged peak	214 265	18 000 17 000	,,
148		H	H	H		80	1660	enlarged peak	214 267	18 500 18 000	,,

TABLE III (Continued)

Code No.	R^{vi}	R''	R'''	R^{v}	Y'	M.P. °C	I.R. cm^{-1} ν–C(=O) ketone	I.R. cm^{-1} ν–C(=O) amide	U.V. λ Max.	U.V. ε	Activity discovered
149	H_3C, CH, H_3C	H	H	H		94	1670	1650	214 267	19 000 18 000	Antitussive and psychotropic
151	$CH_3-(CH_2)_3$	H	H	H		75	1670	1650	214 268	19 000 18 500	,,
154	H_3C, $CH-CH_2$, H_3C	H	H	H		73	1660	enlarged peak	214 267	19 000 18 000	,,
157	H_3C, $CH-CH_2$, H_3C	H	H	H		98	1665	1650	213 267	18 000 18 000	,,
159	$CH_3-(CH_2)_3$	H	H	H		99	1680	1660	211 257	19 000 15 000	,,
164	$Br-CH_2$	H	H	H		134	1670	1640	214 266	22 000 15 000	,,

TABLE III (Continued)

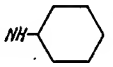
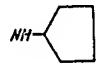
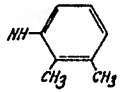
Code No.	R^{vi}	R'''	R''''	R^{v}	Y'	M.P. °C	I.R. cm^{-1} ν–C(=O) ketone	I.R. cm^{-1} ν–C(=O) amide	U.V. λ Max.	U.V. ε	Activity discovered
202	CH_3	H	H	H		106	1660	enlarged peak	214 266	14 000 18 500	Antitussive, psychotropic and analgesic
203	CH_3	H	H	H		99	1680	1640	215 268	14 000 18 500	,,
216	CH_3	H	H	H		170	1670	1640	212 268	24 000 18 500	,,
218	CH_3	H	H	H	$NH-NH_2$	167	1680	1630	215 268	14 000 17 500	,,
219	CH_3	H	H	H		125	1670	1645	212 268	14 000 16 000	,,
223	CH_3	3–CH_3	H	H		117	1670	1650	210 265	19 000 16 000	,,
	CH_3	3–OCH_3	H	H		137					

TABLE III (Continued)

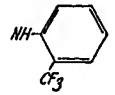
Code No.	R^{vi}	R^{m}	R^{mm}	R^{v}	Y'	M.P. °C	I.R. cm^{-1} ν–C(=O) ketone	I.R. cm^{-1} ν–C(=O) amide	U.V. λ Max.	U.V. ϵ	Activity discovered
256	CH_3	H	H	H		104	1705	1665	210 262	15 000 17 000	Antitussive, psychotropic and analgesic
246	CH_3		H	H		98	1660	1660	245 273	29 000 17 000	,,
263	CH_3		H	H		109	1660	1660	244 270	27 000 16 000	,,
287	CH_3	–2 CH_3	–3 CH_3	H		64	1670	1650	214 267	22 000 13 000	,,
254	CH_3	–2 CH_3	–3 CH_3	H		119	1680	1660	214 267	23 000 13 000	,,
260	CH_3	–2 CH_3	–5 CH_3	H		82	1680	1660	213 268	25 000 15 000	,,
286	CH_3	–2 CH_3	–5 CH_3	H		88	1660	1660	214 268	23 000 15 000	,,

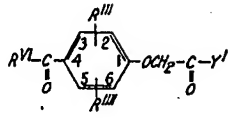
TABLE III (Continued)

Code No.	R^{vi}	R'''	R''''	R^{V}	Y'	M.P. °C	I.R. cm^{-1}		U.V.		Activity discovered
							ν–C– ‖ O ketone	ν–C– ‖ O amide	λ Max.	ε	
261	CH_3	–2 CH_3	H	H		67	1680	1660	217 269	19 000 16 000	Antitussive, psychotropic and analgesic
264	CH_3	–2 CH_3	H	H		107	1680	1660	209 268	20 000 17 000	,,
271	CH_3	–3 OCH_3	H	H		125	1680	1660	264 302	15 000 9 000	,,
275	CH_3	–3 SCH_3	H	H		128	1670	1650	249 276	40 000 16 000	,,
306	CH_3	–3 SCH_3	H	H		130	1660	1660	–	–	,,
309	CH_3	–2 C_2H_5	–5 CH_3	H		95	1660	1660	–	–	,,
318	CH_3	–2 C_2H_5	–5 CH_3	H		96	1670	1650	–	–	,,

TABLE III (Continued)

Code No.	R^{vi}	R'''	R''''	R^{v}	Y′	M.P. °C	I.R. cm^{-1} ν–C–(=O) ketone	I.R. cm^{-1} ν–C–(=O) amide	U.V. λ Max.	U.V. ε	Activity discovered
304	CH_3	H	H	H	NH–CH(CO_2H)–CH_2SH	140	1660	1660	215 265	13 000 17 000	Antitussive, psychotropic and analgesic
	CH_3	–2 Br	H	H		90	–	–	–	–	,,

TABLE IV



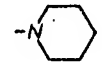
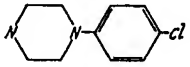
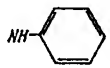
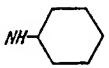
Code No.	R^{vi}	R^{iv}	R^{v}	Y'	M.P. °C	I.R. cm^{-1} ν–C(=O) ketone	I.R. cm^{-1} ν–C(=O) amide	U.V. λ Max.	U.V. ε	Activity discovered
128		H	H		104	1670	1650	211 283	22 000 18 000	Antitussive and psychotropic
129		H	H		129	1675	1650	211 283	20 000 16 000	,,
131		H	H		140	1650		211 255	41 000 40 000	,,
168		H	H		130	1680	1650	245 280	22 000 19 000	,,
167		H	H		116	1690	1660	210 282	14 000 15 000	,,
174		H	H		130	1650		210 283	16 000 17 500	,,

TABLE IV (Continued)

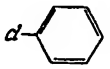
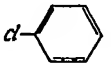
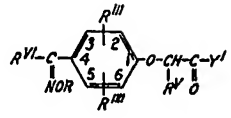
Code No.	R^{vi}	R'''	R''''	Y'	M.P. °C	I.R. cm^{-1}		U.V		Activity discovered
						ν–C–‖O ketone	ν–C–‖O amide	λ Max.	ε	
237		H	H		140	1665	1645	208 288	25 000 18 000	Antitussive and psychotropic
248		H	H		130	1665	1645	207 286	26 000 19 000	,,

TABLE V



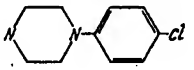
Code No.	R^{vi}	R_o	R'''	R''''	R^{v}	Y'	M.P. °C	I.R. cm^{-1}		U.V.		Activity discovered
								ν OH oxime	ν–C– ‖ O amide	λ Max.	ε	
125		H	H	H	H		172	3250	1640	211 255	45 000 40 500	Sedative, antiinflammatory, analgesic and antitussive
127	$CH_3–CH_2–CH_2$	H	H	H	H		147	3250	1645	212 257	22 000 18 000	,,
130		H	H	H	H		136	3250	1650	212 240	26 000 16 000	,,
132	$CH_3–CH_2–CH_2$	H	H	H	H		159	3250	1645	212 258	19 500 16 000	,,
135	$CH_3–CH_2$	H	H	H	H		144	3300	1660	211 257	22 000 18 000	,,

TABLE V (Continued)

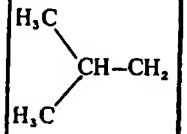
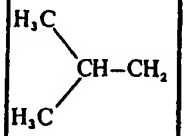
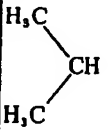
Code No.	R^{vi}	R_o	R'''	R''''	R^v	Y'	M.P. °C	I.R. cm^{-1} ν OH oxime	I.R. cm^{-1} ν–C(=O) amide	U.V. λ Max.	U.V. ε	Activity discovered
147	CH_3-CH_2	H	H	H	H		150	3300	1635			Sedative, antiinflammatory, analgesic and antitussive
152	$CH_3-(CH_2)_3$	H	H	H	H		144	3350	1650	212 268	19 000 15 000	
155		H	H	H	H		124	3300	1635			,,
156		H	H	H	H		147	3300	1640			,,
160		H	H	H	H		142	3150	1635	212 243	18 000 10 000	,,
161	$CH_3-(CH_2)_3$	H	H	H	H		132	3200	1640	213 266	21 000 21 000	,,

TABLE V (Continued)

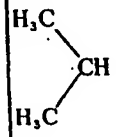
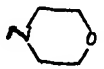
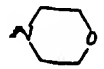
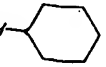
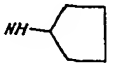
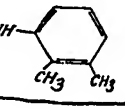
Code No.	R^{vi}	R_o	R'''	R''''	R^V	Y'	M.P. °C	I.R. cm^{-1} ν OH oxime	I.R. cm^{-1} ν–C–(=O) amide	U.V. λ Max.	U.V. ε	Activity discovered
177		H	H	H	H		170	3350	1660	210 242	18 000 10 000	Sedative, antiinflammatory, analgesic and antitussive
179	Br–CH_2	H	H	H	H		182	3350	1630	215 259	29 000 16 000	Analgesic, antitussive and anti-inflammatory
181		H	H	H	H		184	3350	1630	212 238	27 000 19 000	,,
183		H	H	H	H		200	3200	1640	210 264	25 000 18 000	,,
185		H	H	H	H		194	3250	1640	240 263	15 000 15 000	,,
214	CH_3	H	H	H	H		216	3250	1660	209 254	29 000 17 500	Active on the CNS

TABLE V (Continued)

Code No.	R^{vi}	R_o	R'''	R''''	R^V	Y'	M.P. °C	I.R. cm^{-1}		U.V.		Activity discovered
								ν OH oxime	ν–C–(=O) amide	λ Max.	ε	
220	CH_3	H	–3 CH_3	H	H		142	3300	1650	210 240	24 000 9 000	Antitussive and psychotropic
236	H	H	H	H	H		130	3200	1620	210 265	23 000 21 000	,,
279	CH_3	H	H	H	H		162	3300	1640	210 257	21 000 19 000	,,
295		H	H	H	H		202	3300	1640	211 241	25 000 17 000	,,
258	CH_3	H	–3 CH_3	H	H		133	3300	1640	211	22 000	,,
245	CH_3	H	–2 CH_3	–6 CH_3	H		164	3250	1630	212 255	40 000 15 000	,,
247	CH_3	H		H	H		153	3200	1640	208 242	30 000 30 000	,,

TABLE V (Continued)

Code No.	R^{vi}	R_o	R'''	R''''	R^v	Y'	M.P. °C	I.R. cm^{-1}		U.V.		Activity discovered
								ν OH oxime	ν–C– ‖ O amide	λ Max.	ε	
250	CH_3	H		H	H		166	3200	1640	211 242	27 000 29 500	Antitussive and psychotropic
262	CH_3	H	–2 CH_3	–3 CH_3	H		149	3250	1640	212	28 000	,,
252	CH_3	H	–2 CH_3	–3 CH_3	H		166	3250	1640	212	24 000	,,
255	CH_3	H	–2 CH_3	H	H		200	3250	1640	212 258	27 000 17 000	,,
257	CH_3	H	–2 CH_3	H	H		188	3250	1630	213 259	25 000 17 000	,,
274	CH_3	H	–3 SCH_3	H	H		163	3200	1640	225	25 000	,,
265	CH_3	H	–3 SCH_3	H	H		167	3250	1640	223	23 000	,,
284	CH_3	H	–3 OCH_3	H	H		154	3250	1630	245 282	11 000 4 000	,,

TABLE V (Continued)

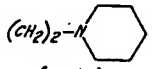
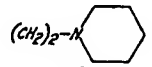
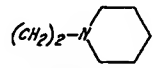
Code No:	R^{vi}	R_o	R'''	R''''	R^v	Y'	M.P. °C	I.R. cm^{-1} ν OH oxime	I.R. cm^{-1} ν–C–(=O) amide	U.V. λ Max.	U.V. ε	Activity discovered
283	CH_3	H	–3 OCH_3	H	H		153	3300	1640	245 283	11 000 4 000	Antitussive and psycho-tropic
300	CH_3	H	–2 CH_3	–5 CH_3	H		140	3250	1630	213	26 000	,,
292	CH_3	H	–2 CH_3	–5 CH_3	H		146	3250	1640	213	26 000	,,
281	CH_3	 *fumarate*	–3 CH_3	H	H		125	–	1620	213	36 000	,,
251	CH_3	 *oxalate*	H	H	H		130	–	1640	213 263	24 000 20 000	,,
277	CH_3	CH_2–CHOH–CH_2OH	H	H	H		110	–	1640	210 260	23 000 20 000	,,
280	CH_3	 *fumarate*	H	H	H		125	–	1630	211 262	35 000 20 000	,,

TABLE V (Continued)

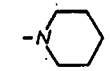
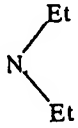
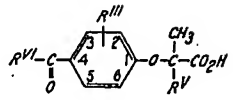
Code No.	R^{vi}	R_o	R'''	R''''	R^v	Y'	M.P. °C	I.R. cm^{-1}		U.V.		Activity discovered
								ν OH oxime	ν–C– ‖ O amide	λ Max.	ϵ	
317	CH_3	H	$-2\ C_2H_5$	$-5\ CH_3$	H		195	3300	1630			Antitussive and psychotropic
320	CH_3	CH_3	H	H	H		126	–	1660			,,
	CH_3	H	H	H	H		126	3250	1620			,,

TABLE VI



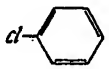
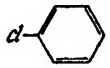
Code No.	R^{vi}	R^{iii}	R^{v}	M.P. °C	I.R. cm^{-1}		U.V.		Activity discovered
					ν–C– ‖ O ketone	ν–C– ‖ O acid	λ Max.	ε	
198	CH_3–CH_2–CH_2–CH_2	H	CH_3	62	1670	1720	215 269	13 000 19 000	Normolipemiant
153		H	CH_3	184	1640	1710	259 294	13 000 17 000	,,
243	CH_3	–3 CH_3	CH_3	98	1640	1735	222 271	15 000 17 000	,,
	CH_3		CH_3	106	1660	1710	–	–	,,
305		H	C_2H_5	140	1630	1740	258 294	13 000 16 000	,,

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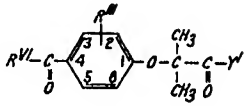
TABLE VII



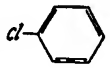
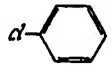
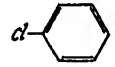
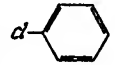
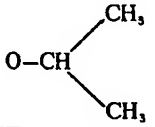
Code No.	R^{vi}	R'''	Y'	B.P. or M.P. °C	I.R. cm^{-1} ν–C–(=O) ketone	I.R. cm^{-1} ν–C–(=O) ester or amide	U.V. λ Max.	U.V. ε	Activity discovered
140	CH_3	H	O–CH_3	M.P. = 62	1670	1730	215 267	12 000 17 000	Normolipemiant
162		H	O–CH_3	M.P. = 89	1660	1740	207 284	13 000 12 000	,,
163		H	O–C_2H_5	M.P. = 79	1665	1735	208 285	19 000 18 000	,,
170		H		M.P. = 160	1650	1620	208 287	24 000 18 000	,,
171		H		M.P. = 148	1650	1640	210 285	25 000 20 000	,,
190		H		M.P. = 84	1660	1730	207 284	18 500 18 000	,,

TABLE VII (Continued)

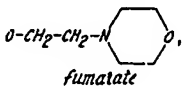
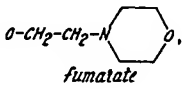
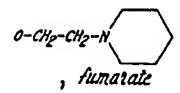
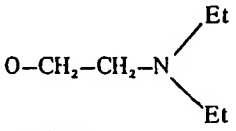
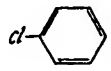
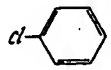
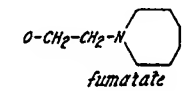
Code No.	R^{vi}	R^{m}	Y'	B.P. or M.P. °C	I.R. cm^{-1} ν–C–(=O) ketone	I.R. cm^{-1} ν–C–(=O) ester or amide	U.V. λ Max.	U.V. ε	Activity discovered
209		H	 fumarate	M.P. = 118	1655	1740	208 282	44 000 20 000	Normolipemiant and cardio-vascular
210	CH_3	H	 fumarate	M.P. = 134	1670	1740	212 265	32 000 12 000	Normolipemiant
211		H	 , fumarate	M.P. = 115	1650	1740	208 184	33 000 17 000	Normolipemiant and cardio-vascular
212		H	 maleate	M.P. = 62	1660	1740	209 283	35 000 18 000	Normolipemiant
217		H		M.P. = 135	1645	1760	—	—	,,
229		H	 fumarate	M.P. = 120	1650	1745	207 285	33 000 16 000	,,

TABLE VII (Continued)

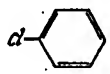
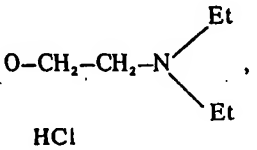
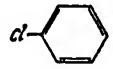
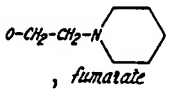
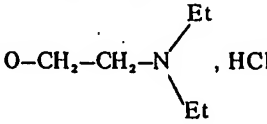
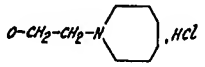
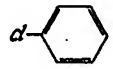
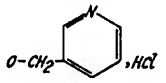
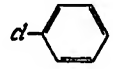
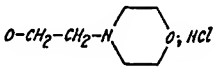
Code No.	R^{vi}	R'''	Y'	B.P. or M.P. °C	I.R. cm^{-1} ν–C(=O)– ketone	I.R. cm^{-1} ν–C(=O)– ester or amide	U.V. λ Max.	U.V. ε	Activity discovered
230		H	 HCl	M.P. = 104	1650	1730	206 286	22 000 17 500	Normolipemiant
231		H	 , *fumarate*	M.P. = 116	1645	1730	208 284	26 000 14 000	,,
232	CH_3–$(CH_2)_3$	H	 , HCl	M.P. = 72	1675	1740	214 267	12 000 16 000	,,
233	CH_3–$(CH_2)_3$	H		M.P. = 118	1675	1740	212 267	12 500 16 000	,,
238		H		M.P. = 144	1660	1740	259 285	20 000 19 000	,,
239		H		M.P. = 145	1645	1740	208 286	20 000 16 000	,,

TABLE VII (Continued)

Code No.	R^{vi}	R'''	Y′	M.P. or B.P. °C	I.R. cm^{-1} ν–C(=O)– ketone	I.R. cm^{-1} ν–C(=O)– ester or amide	U.V. λ Max.	U.V. ε	Activity discovered
240	CH_3	–3 CH_3	O–CH_3	$B.P._{0.05}$ = 132	1680	1745	208 267	17 000 15 500	Normolipemiant
241	CH_3	–3 CH_3	O–C_2H_5	$B.P._{0.05}$ = 136	1680	1740	208 267	16 000 16 200	,,
242	CH_3	–3 CH_3	O–CH(CH$_3$)$_2$	$B.P._{0.05}$ = 139	1680	1730	208 269	17 000 16 200	,,
253	*cl*–C$_6$H$_4$–	–3 CH_3	O–CH(CH$_3$)$_2$		1660	1730	211 257	22 700 18 000	,,
297	*cl*–C$_6$H$_4$–	H	O–CH_2–O_2C–C(CH$_3$)$_2$–CH_3	M.P. = 80	1640	1740	207 284	17 000 16 500	,,
	CH_3	–3 SCH_3	O–CH(CH$_3$)$_2$	BP_1 = 198	1650	1720	–	–	,,

TABLE VII (Continued)

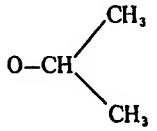
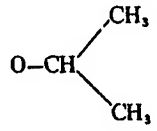
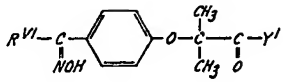
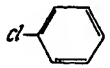
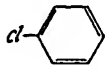
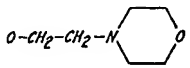
Code No.	R^{vi}	R'''	Y'	M.P. or B.P. °C	I.R. cm^{-1} ν–C(=O)–		U.V.		Activity discovered
					ketone	ester or amide	λ Max.	ε	
	CH_3	$-3\ SO_2CH_3$		M.P. = 86	1690	1720	–	–	Normolipemiant
	CH_3			M.P. = 95	1660	1710	–	–	,,

TABLE VIII

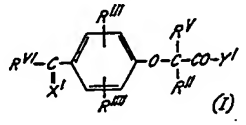


Code No.	R^{vi}	Y^{i}	M.P. °C	I.R. cm^{-1}		U.V.	
				ν OH oxime	–C– ester ‖ or O amide	λ Max.	ε
122	CH_3	$O-C_2H_5$	106	3200	1730		
146	CH_3	$O-CH_3$	102	3200	1730		
172			184	3260	1620	210 247	32 000 20 000
173			175	3280	1620	211 246	31 000 20 000
289			139	3300	1740	–	–

We make no claim to the compounds claimed in the specification of our prior co-pending Application No. 3085/70 (1,268,321), which are defined at the beginning of the specification. Subject to this disclaimer,

WHAT WE CLAIM IS:—

1. A phenoxy-alkyl-carboxylic compound of the general formula:



(I)

in which each of R″ and Rᵛ, which may be identical or different, is a hydrogen atom or a methyl, ethyl, phenyl, *p*-chlorophenyl or *p*-fluorophenyl group; each of R‴ and R⁗, which may be identical or different, is a hydrogen or halogen atom or a C_{1-5} alkyl, CF_3, SCH_3, $SOCH_3$, SO_2CH_3, OCH_3, OH, C_6H_5 or substituted phenyl group; R^{vi} is a hydrogen atom, a C_{1-5} alkyl group, an aryl group optionally containing one or more nuclear substituents selected from methyl and trifluoromethyl groups and halogen atoms, a cycloalkyl, hydroxyl or C_{1-4} alkoxy group, an aryloxy group optionally containing one or more nuclear substituents, or a cycloalkoxy, cycloalkenyloxy, NR_3R_4, $NHCH_2CH_2NR_3R_4$ or O-alkylene-NR_3R_4 group; Y′ is a hydroxy, C_{1-4} alkoxy, $—NR_3R_4$, $—NHCH_2CH_2NR_3R_4$ or O-alkylene-NR_3R_4 group; X′ represents O or NOR_o; R_o is a hydrogen atom or a C_{1-5} alkyl, $—CH_2CH_2NR_3R_4$ or $—CH_2CHOHCH_2OH$ group; and each of R_3 and R_4, which may be identical or different, is a hydrogen atom, a C_{1-5} alkyl or C_{3-7} cycloalkyl group or an aryl group optionally containing one or more nuclear substituents selected from halogen atoms and methyl and trifluoromethyl groups, or R_3 and R_4 together with the nitrogen atom to which they are attached represent an optionally substituted 5- to 7-membered heterocyclic ring which may contain a second heteroatom selected from O, S and N, or radical of formula $—NH(CH_2)_4CH(NH_2)COOH$ or —NH—CH(COOH)—CH_2SH, with the provisos that if R‴ and R⁗ are not both hydrogen, then R^{vi} is methyl or *p*-chlorophenyl, and that if Y′ is hydroxy or alkoxy, R^{vi} is hydrogen or C_{1-5} alkyl and one of R″ and Rᵛ is hydrogen, the other of R″ and Rᵛ is methyl or ethyl.

2. A compound according to Claim 1, in which each of R″ and Rᵛ is a hydrogen atom or a methyl or phenyl group, each of R‴ and R⁗ is a hydrogen or chlorine atom or a methyl, trifluoromethyl or methoxy group, R^{vi} is a straight- or branched-chain C_{1-4} alkoxy group or a hydroxyl, amino, monoalkylamino, di(C_{1-5} alkyl)amino, piperidino, morpholino, azepino, pyrrolidino, piperazino, N′-*p*-chlorophenylpiperazino, aminoalkoxy, mono- or dialkylaminoalkoxy, piperidino alkoxy, morpholinoalkoxy, azepinoalkoxy, piperazinoalkoxy, aryloxy, *p*-chlorophenoxy cyclohexyloxy, Δ^1-cyclohexenyloxy, or $NHCH_2CH_2NR_3R_4$ group; Y′ is a hydroxyl, C_{1-4} alkoxy, NR_3R_4, $—NHCH_2CH_2NR_3R_4$, O—C_{1-6} alkylene-NR_3R_4 or cycloalkylamino group or an arylamino group optionally containing one or more nuclear substituents selected from chlorine atoms and methyl and trifluoromethyl groups; X′ represents O, and either each of R_3 and R_4 is a hydrogen atom or a C_{1-5} alkyl group, or R_3 and R_4, together with the nitrogen atom to which they are attached, represent an optionally substituted 5- to 7- membered heterocyclic ring, which may contain a second heteroatom selected from O, S and N, or radical of formula $NH(CH_2)_4CH(NH_2)COOH$ or —NH—CH(COOH)—CH_2SH.

3. A compound according to Claim 2, in which R^{vi} is a phenoxy group.

4. A compound according to Claim 1, in which each of R″ and Rᵛ is a hydrogen atom or a methyl or phenyl group, each of R‴ and R⁗ is a hydrogen or chlorine atom or a methyl, trifluoromethyl or methoxy group, R^{vi} is a hydrogen atom, a straight- or branched-chain C_{1-5} alkyl group, or an aryl, *p*-chlorophenyl, cyclohexyl or Δ^1-cyclohexenyl group, Y′ is a hydroxyl, C_{1-4} alkoxy, $—NR_3R_4$, $—NHCH_2CH_2NR_3R_4$, O—C_{1-4} alkylene-NR_3R_4 or cycloalkylamino group or an arylamino group optionally containing one or more nuclear substituents selected from chlorine atoms and methyl and trifluoromethyl groups, R_o is a hydrogen atom or a C_{1-5} alkyl or $CH_2CH_2NR_3R_4$ group, and R_3 and R_4 are as defined in Claim 2, with the provisos set forth in Claim 1.

5. A compound according to claim 4, in which R″ is a phenyl group.

6. A compound according to claim 1, in which each of R‴ and R⁗ is a fluorine, chlorine or bromine atom.

7. A compound according to Claim 1 or 6, in which Y′ is a C_{1-4} alkoxy group.

8. A compound according to claim 1, 6 or 7, in which R_6 is a C_{1-5} alkyl group.

9. A compound according to claim 1, 6, 7 or 8, in which NR_3R_4 is amino, mono- or dialkylamino, morpholino, thiomorpholino, pyrrolidino, piperidino, azepino, piperazino, N-*p*-chlorophenyl-piperazino, N-methylpiperazino, 4-methylpiperidino, anilino, 2,3-dimethylanilino, *p*-chloroanilino, O-trifluoromethylanilino, *p*-trifluoromethylanilino, cyclohexylamino, cyclopentylamino or N-methylanilino.

10. N-(*p*-propionyl-phenoxyacetyl)-morpholine.

11. N-(*p*-benzoyl-phenoxyacetyl)-piperidine.

12. N-(*p*-propionhydroximoyl-phenoxyacetyl)-piperidine.

13. Isopropyl *p*-(4-chlorobenzoyl)-phenoxy-isobutyrate.

14. *p*-(4-chlorobenzoyl)-phenoxy-isobutyric acid.

15. N-(*p*-carboxyphenoxy-acetyl)-piperidine.

16. Ethyl *p*-piperidinocarbonyl-phenoxy-acetate.

17. N-(*p*-ethoxycarbonyl-phenoxy-acetyl)-piperidine.

18. An acid addition salt of a compound according to any one of claims 1—9.

19. A compound according to claim 1 or 18 substantially as hereinbefore described.

20. A therapeutical composition comprising a pharmaceutically effective amount of at least one compound according to any one of claims 1, 6—9, 18 and 19.

21. A therapeutical composition comprising a pharmaceutically effective amount of at least one compound according to any one of claims 2, 3 and 15—17.

22. A therapeutical composition comprising a pharmaceutically effective amount of at least one compound according to any one of claims 4, 5 and 10—14.

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London WC1V 7RD.

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